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09/714,865	11/16/2000	Diego H Castrillon	B0801/7195	4880

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	19

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,865	CASTRILLON, DIEGO H	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,22* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1, 3, 4 and 22 have been amended. Claims 1-4 and 22 are pending and under consideration.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. The rejection of claims 1, 4 and 22 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons of record.

Claim 1 is drawn to an isolated nucleic acid molecule selected from the group consisting of nucleic acid which hybridize under stringent conditions to a molecule consisting of a nucleic sequence set forth as SEQ ID NO:1 which code for a vasa polypeptide, and degenerate coding sequences and complements thereof. Claim 4 is drawn to an isolated nucleic acid molecule selected from unique fragments of SEQ ID NO:1. It is noted that claim 4 is rejected under 112, second paragraph for vague and indefinite language. The instant claims are drawn to polynucleotide sequences which hybridize under "stringent" conditions to SEQ ID NO:1 and complements of SEQ ID NO:1. The specification defines "stringent" conditions on page 11 lines 1-12 as encompassing washing of the membrane after hybridization with 0.1 X SSC or 0.1 SDS at temperatures up to 68 degrees. It is recognized in the art that low temperature wash conditions decrease the stringency of the hybridization. Thus, the conditions recited in the specification encompass low stringency and high stringency wash temperatures. The claim carries the limitation that the hybridizing polynucleotides must encode a vasa polypeptide, however, the specification defines a vasa polypeptide as being encoded by a nucleic acid which hybridizes to SEQ ID NO:1. The specification further contemplates that nucleic acids which encode a "respective human vasa polypeptide" having deletions and addition and substitutions to the vasa polypeptide encoded by the nucleic acids which hybridize to SEQ ID NO:2 are included in the present invention as vasa polypeptides (page 10, lines 18-22). The specification states that human vasa is an isolated nucleic acid of SEQ ID NO:1 which codes for a protein which is

specifically expressed in the gonads (page 9, line 23-25). The specification contemplates homologs and alleles of the human vasa nucleic acids as part of the instant invention which can be isolated by hybridization under stringent conditions to SEQ ID NO:1 (page 10, line 31 to page 11, line 12). The specification also contemplates variants of the human vasa which retain the function of the natural human vasa polypeptides as well as dominant-negative vasa polypeptides which do not retain the function of the natural human vasa polypeptide (page 20, lines 4-31). Thus, when given the broadest reasonable interpretation, the claims drawn to hybridizing nucleic acids encompass not only degenerate coding sequences of SEQ ID NO:1, but homologs and alleles, variant and dominant-negative mutants of human vasa. It is concluded that the claims are drawn to a genus of nucleic acids which is highly variant as said genus encompasses polynucleotides encoding polypeptides having numerous structural and functional attributes. The specification describes human vasa polypeptide as SEQ ID NO:2 encoded by the polynucleotide of SEQ ID NO:1. The specification also describes SEQ ID NO:15 as comprising 13 additional nucleotides on the 5' end and 38 nucleotides on the 3' end of SEQ ID NO:1. The specification fails to describe mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:1 relates to the structure of any strictly neutral alleles. The general knowledge in the art is that alleles are variant structures and the structure of one allele is not representative of unknown alleles. Further, the specification does not describe dominant negative mutants of SEQ ID NO:1 or indicate where the mutation would be located. The general knowledge and skill in the art does not supplement the omitted description because specific, not general description is required. Thus, one of skill in the art would reasonably conclude that applicant did not disclose a representative number of species within the genus, as SEQ ID NO:1 does not sufficiently describe the claimed genus because of the structural and functional variation permitted within the genus. Thus, applicant was not in possession of the claimed genus.

Applicant has amended claim 1 to recite specific hybridization conditions. however, the claims fails to specify the wash conditions, and the specification teaches washing of the membrane after hybridization with 0.1 X SSC or 0.1 SDS at temperatures "up to" 68 degrees. It is recognized in the art that low temperature wash conditions, such as those below 68 degrees decrease the stringency of the hybridization. Thus, the conditions recited in the specification

encompass low stringency and high stringency wash temperatures. Therefore the conditions of hybridization recited in the claim to not limit the structure or the nucleic acids which hybridize to SEQ ID NO:1. Further, applicant argues that claim 3 further limits the subject matter of claim 1 in response to the objection to claim 3. It must be deduced from this argument that claim 1 is not limited to nucleic acids of the same length as SEQ ID NO:1. Thus, when given the broadest reasonable interpretation, claim 1 encompasses fragments of varying length which can hybridize to SEQ ID NO:1 under conditions which encompass a low stringency wash. For the reasons set forth above, the disclosure of SEQ ID NO:1 or 15 does not adequately describe the claimed genus, because the genus is highly variant encompassing nucleic acids having numerous structural and functional attributes.

Applicant argues that the specification provides a number of species by way of description of hybridization conditions and the use thereof as well as degenerate nucleotide and conservative substitution. This has been considered but not found persuasive. firstly, claim 1 is much broader in scope that "degenerate coding sequences thereof". Secondly, as stated above, the specification discloses SEQ ID NO:1 as coding for a protein which is specifically expressed in the gonads (page 9, line 23-25). The specification contemplates homologs and alleles of the human vasa nucleic acids as part of the instant invention which can be isolated by hybridization under stringent conditions to SEQ ID NO:1 (page 10, line 31 to page 11, line 12), however, the specification fails to define stringent conditions in terms of the washing step after the hybridization, and includes wash temperatures "up to" 68 degrees, thus encompassing nucleic acids which differ significantly in structure from the disclosed nucleic acids. The specification also contemplates variants of the human vasa as dominant-negative vasa polypeptides which do not retain the function of the natural human vasa polypeptide (page 20, lines 4-31). Thus, the invention includes nucleic acid variants which do not encode proteins having the same activity as the protein encoded by SEQ ISD NO:1. The specification does not disclose any other nucleic acid sequences. The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e.,

complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original). note that a partial structure must be combined with a correlation between function and structure. The claims encompass nucleic acids which hybridize to SEQ ID NO:1 without limiting the function of the nucleic acid or the encoded protein. The specification clearly contemplates variants of SEQ ID NO:1 which differ in function from the protein encoded by SEQ ID NO:1. Thus, the claims do not characterize the genus of nucleic acids claimed in terms of a partial structure with a correlation between function and structure.

Applicant argues that the specification is written for one of ordinary skill in the art and therefore the proper inquiry is whether the specification has described a number of species through the various descriptions of nucleic acid species which would convey to a person of ordinary skill in the art that applicant was in possession of the claimed invention . this has been considered but nor found persuasive. The "proper inquiry" is whether the disclosure as filed provides adequate written description for the genus of nucleic acid claimed. This genus is characterized in terms of structural and functional p[properties of the nucleic acids species that fall within the genus. Because the genus is highly variant, the disclosure of SEQ ID NO:1 or SEQ ID NO:15 which are only two examples of structural attributes and comprise only one example of a functional attribute (encoding a vasa polypeptide which has the same activity as the vasa polypeptide encoded by SEQ ID NO:1) fails to adequately describe the claimed genus.

4. The objection to claim 3 for failing to further limit the scope of claim 1 is withdrawn in light of aplicant arguments.

Applicant argues that the examiner has erroneously contended that SEQ ID NO:15 is larger than SEQ ID NO:1, and that this led to the objection of claim 3 as not further limiting claim 1. Firstly, the examiner made a typographical error and stated the opposite, as SEQ ID NO:1 comprises 13 additionally nucleotides on the 5' end and 38 additional nucleotides on the 3' end of SEQ ID NO:15.. However, claim 3 was objected to because it included fragments of SEQ ID NO:15 and the examiner was questioning if said fragments were indeed a part of claim 1, or if

fragments represented additional nuclide sequences claimed in claim 3. In light of applicants arguments, it is clear that claim 1 encompasses fragments of SEQ ID NO:1 having any length.

5. The rejection of claims 4 and 22 under 35 U.S.C. 112, second paragraph is withdrawn in light of applicant amendments.

Applicant argues that the rejection of claim 4 under 112 second paragraph was unclear. However, the rejection was very clear and centered around the term "unique" which applicant has canceled in response to the rejection, thus rendering said rejection moot.

6. The rejection of claims 1 and 3 under 35 U.S.C. 102(b) as being anticipated by The New England Biolabs Catalog (1994, page 91) is maintained for reasons of record. Claim 22 is also rejected for the same reasons of record. Claim 1 is drawn to an isolated nucleic acid molecule selected from the group consisting of nucleic acid which hybridize under stringent conditions to a molecule consisting of a nucleic sequence set forth as SEQ ID NO:1 which code for a vasa polypeptide, and degenerate coding sequences and complements thereof. Claim 3 is drawn to a fragment of SEQ ID NO:15. Claim 22 is drawn to kit comprising an agent that selectively binds to the isolated nucleic acid of claim 1.

The New England Biolabs Catalog discloses Random Primers on page 91 which would be complementary to the nucleic acids which hybridize under stringent conditions to SEQ ID NO:1, or nucleic acid that differ in genetic code from said nucleic acids, thus fulfilling the specific embodiments of claim 1, section c. The product disclosed by New England Biolabs is a kit because it would comprise the random hexamers within a container and also comprise instructions for use, thus fulfilling the specific embodiments of claim 22. The random hexamers would be a fragment of SEQ ID NO:15 Amendment of claim 1 to recite full length complements of sections (a) or (b) does not suffice to overcome this rejection because claim 1 is clearly drawn to fragments which hybridize to SEQ ID NO:1, as evidenced by applicants arguments regarding claim 3, which is drawn to fragments of SEQ ID NO:15, which applicant vigorously contends further limits the scope of claim 1. Thus, as claim 1 reads on small fragments which hybridize to SEQ ID NO:1, the limitation of "full length complements" in

section c does not exclude full length complements to random hexamers, because random hexamers are encompassed by section(a) and (b).

7. The rejection of claim 4 under 35 U.S.C. 102(b) as being anticipated by Hloch et al (Nucleic Acids Research, 1990, Vol. 18, page 3045) as evidenced by Lemaire et al (Life Sciences, 1993, Vol. 52, pp. 917-9260) and Castrillon et al (PNAS, 2000, Vol. 97, pp. 9585-9590) is maintained for reasons of record.

It is noted that claim 4 is drawn to an isolated nucleic acid molecule selected from fragments between 8 and 2223 nuclides of SEQ ID NO:1 or full length complements thereof., but does not specifically state if the nucleic acid molecule comprises or consists of said fragments.

Hloch et al disclose the polynucleotide and polypeptide sequence of human p68. Lemaire et al disclose that vasa and p68 and mouse PL10 share conserved protein segments(page 554, second column, under the heading "PL10 Deduced Protein Shares Similarities with Murine elF-4A and Other Proteins"). Lemaire et al disclose that similarity between human p68 and other proteins encoding RNA helicases which are expressed within male germ cells is high in the region of the dead motif (table 1, page 921). Castrillon et al disclose that the human vasa gene contains a DEAD motif (page 9586, second column, lines 4-6 under the heading "Comparison of the Predicted Human VASA Protein Sequence with Other Species"). Thus, it is reasonable to conclude that the human p68 gene disclosed by Hloch et al comprises a DEAD motif having a unique fragment of SEQ ID NO:1. It is noted that murine p68, but not human p68 is excluded from claim 4.

The added limitation of "8 and 2223 nucleotides in length" fails to obviate this prior art rejection, because the DEAD motif would be between 8 and 2223 nucleotides in length

Claims drawn to fragments of a nucleic acid will read as nucleic acids comprising said fragments in the absence of specific language that requires the nucleic acid to "consist of" a specific fragment.

8. Claim 2 remains objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. All other rejeections and objections as set forth in Paper No. 12 are withdrawn.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner, Group 1642
11/25/03